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FROM: Martha A. Robinson**USER ID:** MR10031 **FLOOR:** 20**PHONE:** (512) 536-5616**FAX:** (512) 536-4598**RE:** RESUBMISSION OF IDS AND FORM PTO-1449**NUMBER OF PAGES WITH COVER PAGE:** 16 **Originals Will Not Follow****Message:**

U.S. Application No. 09/506,988 entitled "PROTEASE INHIBITORS THAT OVERCOME DRUG RESISTANCE" by Tang and Ghosh.

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Steven L. Highlander

D. Margaret Seaman, Examiner
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

RE: *U.S. Patent Application No. 09/506,988 entitled "PROTEASE INHIBITORS THAT
OVERCOME DRUG RESISTANCE" — Jordan J.N. Tung and Arun K. Ghosh*
Our reference: OMRP:056US
Client reference:

Dear Examiner Seaman:

After reviewing each of the Office Actions and the Notice of Allowability, it has come to our attention that the Information Disclosure Statement, Form PTO-1449 and 57 references submitted on July 25, 2000, were apparently never signed off by an Examiner.

For your convenience we have enclosed a copy of a Supplemental Information Disclosure Statement and Form PTO-1449 that was filed with the Patent and Trademark Office (PTO) on July 25, 2000. Also enclosed is a copy of PTO stamped postcard indicating the documents submitted. The copies of the references previously submitted have not been enclosed. Please let us know if you would like us to resubmit those as well.

Please review and approve this Supplemental Information Disclosure Statement. If you need additional information, please let us know.

Thank you for your assistance in this matter.

Respectfully submitted,

Steven L. Highlander
Reg. No. 37,642

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The "Received" stamp of the Patent Office imprinted hereon acknowledges the filing of:

Applicant(s): Jordan I.N. Tang and Anun K. Ghosh

Serial & Docket Nos.: 09/506,988 OMRF 176

Filed: February 18, 2000

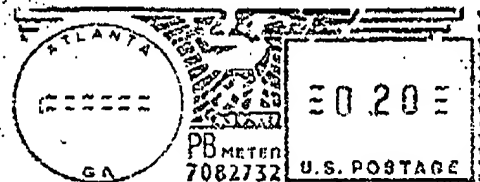
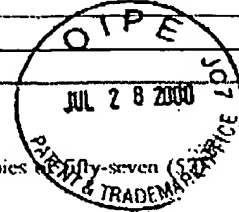
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Information Disclosure Statement, six (6) pages of Form PTO-1449, and copies of fifty-seven (57) documents cited therein.

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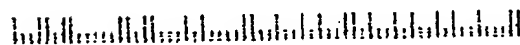
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By: Patrea L. Pabst, Reg. No. 31,284



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Applicants: Jordan J.N. Tang and Arun K. Ghosh

Serial No.: 09/506,988

Art Unit:

Filed: February 18, 2000

Examiner: Not Yet Assigned

For: *PROTEASE INHIBITORS THAT OVERCOME DRUG RESISTANCE*Assistant Commissioner for Patents
Washington, D.C. 20231**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicants submit an Information Disclosure Statement, including six (6) pages of Form PTO-1449 and a copy of each document cited therein.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 01-2507.

Publications

BALDWIN, et al., "Structural basis of drug resistance for the V82A mutant of HIV-1 proteinase," *Nat. Struct. Biol.* 2(3):244-9 (1995).

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Remarks

This statement should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, Applicants invite the Examiner to make an independent evaluation of the cited art to determine its relevance to the subject matter of the present application. Applicants are of the opinion that their claims patentably distinguish over the art referred to herein, either alone or in combination.

Respectfully submitted,



Robert A. Hodges
Reg. No. 41,074

Dated: July 25, 2000

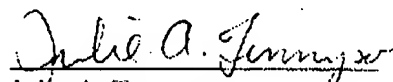
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Julie A. Tennyson

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		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
Sheet 1 of 6	Attorney Docket Number	OMRF 176	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No.†	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	1*
		BAI DWIN, et al., "Structural basis of drug resistance for the V82A mutant of HIV-1 proteinase," <i>Nat. Struct. Biol.</i> 2(13):244-9 (1995).	
		BOGER, "Renin Inhibitors. Design of Angiotensinogen Transition-state Analogs Containing Statine: Conformationally restricted inhibitors and a model for the bound conformation of renin substrate," in <i>Aspartic Proteinases and Their Inhibitors</i> , (Kostka, V., ed.), pp. 401-420, Walter de Gruyter: N.Y., 1985.	
		CARPENTER, et al., "Antiretroviral therapy for HIV infection in 1998: Updated recommendations of the International AIDS Society-USA Panel," <i>JAMA</i> 280(1):78-86 (1998).	
		CARROLL, et al., "Identification of potent inhibitors of <i>Plasmodium falciparum</i> plasmepsin II from an encoded statine combinatorial library," <i>Bioorg. Med. Chem. Lett.</i> 8(17):2315-20 (1998).	
		CARROLL, et al., "Evaluation of a structure based statine cyclic di-amino amide encoded combinatorial library against plasmepsin II and cathepsin D," <i>Bioorg. Med. Chem. Lett.</i> 8(22):3203-6 (1998).	
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		CONDRA, et al., "In vivo emergence of HIV 1 variants resistant to multiple protease inhibitors," <i>Nature</i> 374(6522):569-71 (1995).	
		CRAIG, et al., "Antiviral properties of Ro 31-8959, an inhibitor of human immunodeficiency virus (HIV) proteinase," <i>Antiviral Res.</i> 16(4):295-305 (1991).	

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		Application Number	09/506,988
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		Group Art Unit	1614
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Sheet 2 of 6	Attorney Docket Number	OMRF 176	

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		DEBOUCK & METCALF, "Human immunodeficiency Virus Protease: A target for AIDS therapy," <i>Drug Devel. Res.</i> 21:1-17 (1990).	
		DEBOUCK, et al., "Human immunodeficiency virus protease expressed in <i>Escherichia coli</i> exhibits autoprocessing and specific maturation of the gag precursor," <i>Proc. Natl. Acad. Sci. USA</i> 84:8903-8907 (1987).	
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		HO, et al., "Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection," <i>Nature</i> 373(6510):123-6 (1995).	

Examiner's Signature	Date Considered
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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
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		Examiner Name	
Sheet 3 of 6	Attorney Docket Number	OMRF 176	

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		DUNN, et al., "Subsite Preferences of Retroviral Proteinases" <i>Methods in Enzymology</i> 241:254-278 (1994).	
		HONG, et al., "Active-site mobility in human immunodeficiency virus, type 1, protease as demonstrated by crystal structure of A285 mutant." <i>Protein Sci.</i> 7(2):300-5 (1998).	
		HONG, et al., "Crystal structures of complexes of a peptidic inhibitor with wild type and two mutant HIV-1 proteases." <i>Biochemistry</i> 35:123-126 (1996).	
		HOOVER, et al., "Discovery of inhibitors of human renin with high oral bioavailability." <i>Adv Exp Med Biol.</i> 362:167-80 (1995).	
		IDO, et al., "Kinetic studies of human immunodeficiency virus type 1 protease and its active-site hydrogen bond mutant A28S." <i>J. Biol. Chem.</i> 266(36):24359-66 (1991).	
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Application Number		09/506,988	
Filing Date		February 18, 2000	
First Named Inventor		Jordan J.N. Tang	
Group Art Unit		1614	
Examiner Name			
Attorney Docket Number		OMRF 176	
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		LIN, et al., "Effect of point mutations on the kinetics and the inhibition of human immunodeficiency type 1 protease: Relationship to drug resistance," <i>Biochemistry</i> 34:1143-1152 (1995).	
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		PATICK, et al., "Antiviral and resistance studies of AG1343, an orally bioavailable inhibitor of human immunodeficiency virus protease," <i>Antimicrob. Agents Chemother.</i> 40(2):292-7 (1996).	
		PENG, et al., "Role of human immunodeficiency virus type 1-specific protease in core protein maturation and viral infectivity," <i>J. Virol.</i> 63(6):2550-6 (1989).	
		POORMAN, et al., "A cumulative specificity model for proteases from human immunodeficiency virus types 1 and 2, inferred from statistical analysis of an extended substrate data base," <i>J. Biol. Chem.</i> 266(22):14554-61 (1991).	

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		RIDKY & LEIS, "Development of drug resistance to HIV-1 protease inhibitors," <i>J. Biol. Chem.</i> 270(50):29621-3 (1995).	
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		TOH, et al., "Is the AIDS virus recombinant?" <i>Nature</i> 316(6023):21-2 (1985).	
		TOMASSELLI, et al., "The complexities of AIDS: An assessment of the HIV protease as a therapeutic target," <i>Chimicaoggi Chemistry Today</i> 9:6-27 (1991).	

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First Named Inventor	Jordan J.N. Tang
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Attorney Docket Number	OMRF 176

Sheet 6 of 6

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		TONG, et al., "Crystal structure of human immunodeficiency virus (HIV) type 2 protease in complex with a reduced amide inhibitor and comparison with HIV-1 protease structures," <i>Proc. Natl. Acad. Sci. USA</i> 90(18):8387-91 (1993).	
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		WEI, et al., "Viral dynamics in human immunodeficiency virus type 1 infection," <i>Nature</i> 373(6510):117-22 (1995).	
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		WLODAWER, et al., "Conserved folding in retroviral proteases: crystal structure of a synthetic HIV-1 protease," <i>Science</i> 245(4918):616-21 (1989).	

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